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			Application Number	09/648,				
TRANS	SMITTAL	1	Filing Date	May 4,	May 4, 2001			
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(to be used for all corre	espondence after initial fill	iing)	Art Unit	1631				
			Examiner Name	Michae	el L. Borin			
Total Number of Pages in	in This Submission	11	Attorney Docket Number	SYRTE	SYRTECH-5001-U			
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Docket No. SYRTECH-5001-U

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APR 2 9 2004

In re Patent Application of

Duncan McRee et al.

Group Art Unit: 1631

Examiner: Borin, Michael L.

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Application No.: 09/848,866

Filed: May 4, 2001

Title: DETERMINING STRUCTURES

BY PERFORMING

COMPARISONS BETWEEN MOLECULAR REPLACEMENT RESULTS FOR MULTIPLE DIFFERENT BIOMOLECULES

RESPONSE TO RESTRICTION AS TO SPECIES

Mail Stop Non-Fee Amendment Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

Sir:

In response to Examiner's Restriction Requirement mailed April 20, 2004, Applicants respectfully request reconsideration of the above-referenced application in view of the following election, amendment, and remarks.

AMENDED SECTIONS

X Claims appear at pages 2-8

REMARKS/ARGUMENTS

X Remarks / Arguments appear at page 9

Docket No. SYRTECH-5001-U

This listing of claims will replace all prior versions and listings of claims in the application.

LISTING OF CLAIMS

1. (original) A method for identifying a search model to use in molecular replacement for determining a structure of a target biomolecule from crystal data, the method comprising:

employing computer executable logic to perform multiple molecular replacement searches on crystal data of the target biomolecule where a group of different biomolecule structures are used as search models for the multiple molecular replacement searches; and

employing computer executable logic to compare solutions from the multiple molecular replacement searches, the comparison producing data from which biomolecule structures in the group can be identified as having superior structural identity with the target biomolecule as compared to the other biomolecule structures in the group.

- 2. (original) A method according to claim 1 wherein comparing molecular replacement solutions comprises comparing figures of merit calculated for the molecular replacement solutions.
- 3. (currently amended) A method according to claim 4 2 wherein comparing molecular replacement solutions comprises performing a statistical analysis on figures of merit calculated for the molecular replacement solutions.
- 4. (currently amended) A method according to claim ± 2 wherein comparing molecular replacement solutions comprises determining which of the biomolecule structures in the group produced a molecular replacement solution whose figure of merit is at least two standard deviations better than the average figure of merit for molecular replacement solutions for the biomolecule structures in the group.

Docket No. SYRTECH-5001-U

- 5. (currently amended) A method according to claim 4 2 wherein comparing molecular replacement solutions comprises determining which of the biomolecule structures in the group produced a molecular replacement solution whose figure of merit is at least three standard deviations better than the average figure of merit for molecular replacement solutions for the biomolecule structures in the group.
- 6. (currently amended) A method according to claim ± 2 wherein comparing molecular replacement solutions comprises determining which of the biomolecule structures in the group produced a molecular replacement solution whose figure of merit is at least five standard deviations better than the average figure of merit for molecular replacement solutions for the biomolecule structures in the group.
- 7. (currently amended) A method according to claim 4 2 wherein comparing molecular replacement solutions comprises determining which of the biomolecule structures in the group produced a molecular replacement solution whose figure of merit is at least ten standard deviations better than the average figure of merit for molecular replacement solutions for the biomolecule structures in the group.
- 8. (original) A method according to claim 1 wherein comparing molecular replacement solutions comprises comparing root mean square errors for each molecular replacement solution of a probability-weighted average over all possible phase choices.
- 9. (original) A method according to claim 1 wherein comparing molecular replacement solutions comprises establishing a background correlation level between the biomolecule structures in the group and the target biomolecule based on the molecular replacement solutions and determining which of the biomolecule structures in the group produced a molecular replacement solution that exceeds the background correlation level by at least two standard deviations.

Docket No. SYRTECH-5001-U

- 10. (original) A method according to claim 1 wherein comparing molecular replacement solutions comprises establishing a background correlation level between the biomolecule structures in the group and the target biomolecule based on the molecular replacement solutions and determining which of the biomolecule structures in the group produced a molecular replacement solution that exceeds the background correlation level by at least three standard deviations.
- 11. (original) A method according to claim 1 wherein comparing molecular replacement solutions comprises establishing a background correlation level between the biomolecule structures in the group and the target biomolecule based on the molecular replacement solutions and determining which of the biomolecule structures in the group produced a molecular replacement solution that exceeds the background correlation level by at least five standard deviations.
- 12. (original) A method according to claim 1 wherein comparing molecular replacement solutions comprises establishing a background correlation level between the biomolecule structures in the group and the target biomolecule based on the molecular replacement solutions and determining which of the biomolecule structures in the group produced a molecular replacement solution that exceeds the background correlation level by at least ten standard deviations.
- 13. (currently amended) A method according to claim 4 2 wherein the group of different biomolecule structures on which molecular replacement searches are performed comprises at least 3 different biomolecule structures.
- 14. (currently amended) A method according to claim 1 2 wherein the group of different biomolecule structures on which molecular replacement searches are performed comprises at least 0.1% of the protein structures stored in the Protein Data Bank.

Docket No. SYRTECH-5001-U

- 15. (currently amended) A method according to claim 4 2 wherein the group of different blomolecule structures on which molecular replacement searches are performed comprises at least one biomolecule structure that has less than 70% sequence identity with the target biomolecule.
- 16. (currently amended) A method according to claim 12 wherein the group of different biomolecule structures on which molecular replacement searches are performed comprises at least two different biomolecule structures that are structurally dissimilar to each other.
- 17. (currently amended) A method according to claim 4 2 wherein the group of different biomolecule structures on which molecular replacement searches are performed comprises at least two different biomolecule structures that have less than 70% sequence identity with each other.
- 18. (currently amended) A method according to claim 4 2 wherein the group of different biomolecule structures on which molecular replacement searches are performed comprises at least one predicted structure for a biomolecule.
- 19. (currently amended) A method according to claim 1 2 wherein the group of different biomolecule structures on which molecular replacement searches are performed comprises at least one structure where at least a portion of the native structure has been removed.
- 20. (currently amended) A method according to claim 4 2 wherein the group of different biomolecule structures on which molecular replacement searches are performed comprises at least one structure which comprises a combination of two or more structure fragments.

21-51 (withdrawn)

Docket No. SYRTECH 5001-U

52. (original) A computer readable medium useful in association with a computer which includes a processor and a memory, the computer readable medium comprising:

logic for performing multiple molecular replacement searches on crystal data of a target biomolecule where a group of different biomolecule structures are used as search models for the multiple molecular replacement searches; and

logic for comparing solutions from the multiple molecular replacement searches, the comparison producing data from which biomolecule structures from the group can be identified as having superior structural identity with the target biomolecule as compared to the other biomolecule structures in the group.

53. (original) A method for identifying a search model to use in molecular replacement for determining a structure of a target biomolecule from crystal data, the method comprising:

employing computer executable logic to perform multiple molecular replacement searches on crystal data of the target biomolecule where a group of different biomolecule structures are used as search models for the multiple molecular replacement searches; and

employing computer executable logic to identify a biomolecule structure from the group whose use as a search model produces a molecular replacement solution that is superior to the molecular replacement solutions produced by the other biomolecule structures in the group.

54. (original) A computer readable medium useful in association with a computer which includes a processor and a memory, the computer readable medium comprising:

logic for performing multiple molecular replacement searches on X-ray diffraction data of a target biomolecule where a group of different biomolecule structures are used as search models for the multiple molecular replacement searches; and

logic for identifying a biomolecule structure from the group whose use as a search model produces a molecular replacement solution that is superior to the

Docket No. SYRTECH 5001-U

molecular replacement solutions produced by the other biomolecule structures in the group.

55. (original) A method for determining a structure of a target biomolecule from crystal data, the method comprising:

employing computer executable logic to perform multiple molecular replacement searches on crystal data of the target biomolecule where a group of different biomolecule structures are used as search models for the multiple molecular replacement searches;

employing computer executable logic to identify a biomolecule structure from the group whose use as a search model produces a molecular replacement solution that is superior to the molecular replacement solutions produced by the other biomolecule structures in the group; and

employing computer executable logic to determine a structure for the target biomolecule employing the identified biomolecule structure.

56. (original) A computer readable medium useful in association with a computer which includes a processor and a memory, the computer readable medium comprising:

logic for performing multiple molecular replacement searches on crystal data of a target biomolecule where a group of different biomolecule structures are used as search models for the multiple molecular replacement searches;

logic for identifying a biomolecule structure from the group whose use as a search model produces a molecular replacement solution that is superior to the molecular replacement solutions produced by the other biomolecule structures in the group; and

logic for determining a structure for the target biomolecule employing the identified biomolecule structure.

Docket No. SYRTECH 5001-U

- 57. (original) A method for identifying a search model to use in molecular replacement for determining a structure of a target biomolecule from crystal data, the method comprising:
- (a) employing computer executable logic to perform multiple molecular replacement searches on crystal data of the target biomolecule using multiple different biomolecule structures as search models;
- (b) employing computer executable logic to compare the resulting molecular replacement solutions in order to identify a biomolecule structure whose use as a search model produces a molecular replacement solution that is superior to the molecular replacement solutions of other biomolecule structures upon which the molecular replacement searches were performed; and
- (c) if none of the molecular replacement solutions are comparatively better, evaluating additional biomolecule structures by repeating steps (a) and (b) with the additional biomolecule structures until a biomolecule structure is identified which produces a molecular replacement solution that is superior to the molecular replacement solutions of other biomolecule structures upon which the molecular replacement searches were performed.

Docket No. SYRTECH 5001-U

REMARKS/ARGUMENTS

The Examiner has issued a restriction requirement alleging that the application claims eight distinct species. Claims 1 and 52-57 were indicated as being generic.

Pursuant to 37 C.F.R. § 1.142, Applicants elect the species directed to determining molecular replacement solutions. Claims 2-12 are directed to this species. Claims 13-20 have been amended to depend from claim 2 and thus now fall within the elected species.

Claims 21-51 are withdrawn as being directed to the non-elected species pursuant to 37 C.F.R. 1.142(b). However, Applicants reserve the right pursuant to 37 C.F.R. § 1.141 to pursue claims to the non-elected species in this application in the event that a generic claim is found to be allowable.

Applicants also reserve the right pursuant to 35 U.S.C. § 121 to file one or more divisional applications directed to the non-elected species during the pendency of the present application.

Docket No. SYRTECH 5001-U

CONCLUSION

Applicants earnestly believe that they are entitled to a letters patent, and respectfully solicit the Examiner to expedite prosecution of this patent application to issuance. Should the Examiner have any questions, the Examiner is encouraged to telephone the undersigned.

Respectfully submitted, Syrrx, Inc.

Dated: April 27, 2004

David J. Weitz, General Counsel & V. P. of Intellectual Property

Reg. No. 38,362

Customer No. 32793 Syrrx, Inc. 10410 Science Center Drive San Diego, CA 92121 Telephone: (858) 622-8528 Facsimile: (858) 550-0992